curvature ulcer after 10 weeks on 1-6-delta-methylhydrocortisone; a barium-meal examination just prior to treatment showed nothing abnormal. With this point in mind I have examined the case histories of all patients with gastric ulcer confirmed by barium-meal examination in the *x*-ray department of the Radcliffe Infirmary during the four years 1957–61. During this period there were two lesser-curvature steroid ulcers, as well as three of the greater-curvature steroid ulcers mentioned in this article. The above facts suggest that steroids are a frequent cause of greater-curvature ulcers. It is therefore important for the radiologist to examine the greater curvature very carefully in patients who are taking steroids; bearing in mind that it is often more difficult to detect ulcers at this site in view of the tendency of barium to "pocket" between the coarser mucosal folds along the greater curvature. An ulcer crater may be dismissed as such a "pocket," as happened in Case 2.

Summary

Four cases of steroid-induced benign greater-curvature gastric ulcers are recorded. There is evidence to suggest that in patients on steroid therapy there is a greater tendency to form ulcers on the greater curvature. Greater-curvature steroid ulcers form a group of greater-curvature ulcers which may be diagnosed as such radiologically and are without exception benign.

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SINGLE-DOSE TREATMENT OF OXYURIASIS WITH PYRVINIUM EMBONATE

BY

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Infection with oxyuris (threadworms) is still an important problem in India. Although oxyuriasis is found more often in children, no age is exempt. The nocturnal pruritus caused by egg-laying in the perianal region is the result of local irritation and inflammation, which may be exaggerated by scratching and superimposed secondary infection (Royer and Berdnikoff, 1962).

Many drugs have been used for their anthelmintic activities against oxyuria. The piperazine group, most commonly used to-day, has to be administered over a period of 7 to 15 days in three daily divided doses to achieve good results.

Early work by Weston *et al.* (1953) indicated the effectiveness of a cyanine dye, later named pyrvinium chloride, against oxyuria. This drug was administered in a seven-day course and showed nearly a 100% cure rate for oxyuria infection in humans. Later when the embonate (pamoate in the U.S.A.) derivative was available. it was shown to be equally effective and virtually non-toxic.

The study reported here was carried out to assess the efficacy of a single dose of pyrvinium embonate ("vanquin") on oxyuria infections.

Material and Method

Patients, both adults and children, of St. George's Hospital, Bombay, who showed oxyuria infection were selected for this study. Adults in- and out-patients and child in-patients were selected for the trial, because it was very difficult to follow paediatric patients with daily Scotch-tape studies on an out-patient basis. Children admitted to the paediatric wards for various illnesses were examined by the Scotch-tape technique, those showing positive results being included in this study. The total number of patients was 150—77 adults (68 males, 9 females) and 73 children (40 males, 33 females). Only those adults who either gave a history of passing oxyuris in stools or whose stools showed adult oxyuris or ova were screened with the Scotch-tape technique. Those showing a positive result were then admitted to the study. Children admitted to the wards for various illnesses were examined by a single Scotch-tape test and those whose test was positive for the ova were admitted to the study. It is conceded that many cases of oxyuriasis must have been missed, but the purpose of this paper was not to determine the incidence of this infection but merely to assess the efficacy of the drug.

The Scotch-tape test was carried out as a modification of the Graham cellulose-tape technique. The adhesive side of a small loop of cellulose tape (Scotch tape) was pressed over the anal and perianal surface of the patient. Usually this procedure was carried out early in the morning. The Scotch tape was then placed with adhesive side down on a drop of toluene on a microscope slide. This preparation was then examined for the ova of *Oxyuris vermicularis*.

Patients who showed positive tape results received a single dose of pyrvinium embonate. Adults received medication in the form of tablets and children a suspension. The individual dose was calculated as 5 mg./kg. of body weight. One tablet of pyrvinium contains 50 mg. of the drug, while the suspension contains 50 mg. per 5 ml., and is a pleasant-tasting strawberry-flavoured liquid which was easily taken by most children.

All patients who received pyrvinium therapy were Scotch-tape-tested daily for 15 days after medication, and watched carefully for any reactions to the drug or for toxic manifestations. Although occasional days of Scotch-taping were missed in some patients, omissions were not frequent enough to affect the results of the

study. About 30 patients who attended the clinic irregularly or failed to return for proper post-therapeutic follow-up were not included in the results.

Results of Clinical Trial

The 150 patients (108 males, 42 females) ranged in age from 2½ to 54 years. They were treated with a single dose of pyrvinium, the dosage being 5 mg./kg. of body weight. Daily Scotch-tape testing was done for 15 days after therapy, and the results of treatment were assessed according to the data obtained. As can be seen in the Table, more than 50% of the patients showed negative tests in 24 hours and the tests remained negative thereafter. By the fifth day nearly 94% of tests became negative, and within a week nearly 98% of tests were negative.

Results of Scotch-taping in 150 Cases for 15 Days After Single-dose Treatment with Pyrvinium Embonate (5 mg./kg.). Number Showing No Oxyuris Ova Daily for 15 Days

Day:	1	2	3	4	5	6	7–15
No. of patients	76	87	105	128	140	146	147
Percentage ..	50·6	58·0	70·0	85·4	93·4	97·4	98·0
No. Scotch-taped	150	150	150	150	149	149	144

Three patients in this series continued to show ova even after two weeks. These three were heavily infested, as shown on the slide in the pretreatment phase. The 15-day post-treatment slide still showed ova although the number was greatly reduced. Each of the three patients then received an additional dose (5 mg./kg.) of pyrvinium two weeks after the first dose and each responded well, with the Scotch-tape test becoming negative after three to six days and remaining negative thereafter.

A few of the patients in the study visited the clinic four to six weeks after therapy and were re-examined for any evidence of further infection. Four patients examined a month after treatment showed negative results, and three examined about six weeks after treatment also showed negative results. Eight patients examined in four to eight weeks after treatment again showed positive Scotch-tape tests and were re-treated with a second dose of pyrvinium with excellent results. Even though all the patients had been instructed to observe the basic rules of personal hygiene, since re-infection is very common with oxyuris, it was likely that cross-infection from other members of the family would occur. It was not possible to treat the whole families because of the difficulty in persuading all the members of the family to attend the clinic daily for Scotch-tape testing.

Two patients treated with pyrvinium on an out-patient basis each showed a negative test on the third day but positive results on the 12th and 13th days, respectively. Perhaps these patients were reinfected. A second dose of pyrvinium was given with excellent response.

Side-effects.—These were remarkably few. All the adults tolerated the drug very well. There were no gastro-intestinal upsets of any kind. Four of the children developed nausea and two others developed vomiting with a mild diarrhoea. All of these children were in an older age-group (10 to 13 years) and were given a fairly large dose of the suspension—15 to 20 ml. It was felt that these side-effects were related to the quantity of pyrvinium suspension administered, since the four who developed nausea were later given an equivalent dose of the drug in tablet form and none of them showed any gastro-intestinal disturbances. No other side-effects were observed. To avoid any undue anxiety, all patients were informed that the stools would become red in colour. There are no known clinical contraindications to the use of pyrvinium (Royer and Berdnikoff, 1962). The makers of the drug state that it is non-toxic to the liver, kidneys, and other organs. Some of the patients who received this drug had concomitant heart, liver, or kidney diseases and in no case was any adverse effect seen.

Effects on Other Intestinal Infections.—Associated roundworm, hookworm, or tape-worm infection was present in 18 of the patients. There were no ill-effects from any of these infections, and the stools remained positive after treatment with pyrvinium was completed. Pyrvinium (5 to 15 mg./kg. as a weekly dose) did not cure a 16-year-old girl of tapeworm. Though the tapeworm was not eradicated, there were no toxic effects from even the large amount of the drug given. Twelve patients had associated amoebic infection with cysts of *Entamoeba histolytica* in their stools. After the single dose of pyrvinium, the cysts continued to appear in the stools. Four of these 12 patients had associated amoebic hepatitis. They all tolerated the drug well without any toxic effects. Although it was not the purpose of this study to observe the effects of pyrvinium in other infections, mention is made of these.

Discussion

It is clear from the above observations that pyrvinium is very efficacious in the eradication of oxyuris and has two special advantages—that of being practically non-toxic, and that of being able to be administered as a single dose either in the form of a tablet or as a pleasant strawberry-flavoured suspension. It can effect a cure rate of nearly 98%. Previous investigators, such as Royer (1956), Miller *et al.* (1958), Bumbalo *et al.* (1958, 1960), and Beck *et al.* (1959), have shown the effectiveness of this drug for oxyuriasis given as either multiple doses or as a single dose. Our study has confirmed the previous reports.

It must be stressed that, since *Oxyuris vermicularis* has a very great potential of producing eggs (estimated from 5,000 to 20,000 eggs per worm), complete eradication must be achieved to cure a patient. In India, oxyuriasis is widespread and often patients are heavily infested. The perianal itching produced by the laying of eggs is very distressing. A swift and complete cure would therefore indicate a significant advance in treatment. Such a result can now be achieved with a single dose of pyrvinium. Reinfection from other members of the family should be prevented by treating all the family with pyrvinium. This family-unit treatment is feasible because the drug is virtually non-toxic and can be administered as a single dose. Furthermore, the drug can be used as a prophylactic measure in an institution where oxyuriasis is shown to be present in a few inmates.

Summary

Pyrvinium embonate is a new drug belonging to the cyanine dye group. In a single dose (5 mg./kg.) it is remarkably effective against oxyuriasis and is virtually non-toxic. Of 150 patients, ranging in age from 2½ to 54 years, treated with this drug, 98% were cured by a single dose. Side-effects were transient and consisted of nausea, vomiting, and mild diarrhoea. These side-effects

occurred in only 6 of the 150 cases (4%) and then only in those who received a relatively large volume of the suspension. The drug was completely non-toxic when given in tablet form.

This drug represents a great improvement on the previously used oxyuricides and can be hailed as a milestone in the treatment of oxyuriasis.

I wish to thank Dr. Mousik, superintendent, St. George's Hospital, Bombay, for allowing me to undertake this study on hospital patients. Thanks are also due to Dr. Nazareth, paediatrician, St. George's Hospital, for allowing me to use his paediatric cases for this study. Finally, thanks are due to Parke, Davis and Company, Detroit, for supplying "vanquin" free of cost.

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Medical Memoranda

Hypoglycaemic Coma During Change from Insulin to Tolbutamide

Since the introduction of tolbutamide as an oral hypoglycaemic agent in 1955, increasing numbers of diabetics have been successfully treated with this drug.

The change from insulin to tolbutamide in a suitable case is usually uneventful, and there may be a temptation to try this without first admitting the patient to hospital. It is not generally recognized that hypoglycaemic coma can occur during the change-over; the rapidity of onset and severity of such a coma is shown in the following case.

CASE REPORT

A 67-year-old woman who was first found to have diabetes at the age of 42 was admitted to hospital on December 24, 1961, because of increasing breathlessness and swelling of the legs and abdomen of six months' duration. For three months she had been having angina of effort, severe orthopnoea, and paroxysms of nocturnal dyspnoea. She also complained of dizziness and confusion and there was difficulty in giving her insulin. Since 1950 she had been stable on a diet of 10 black and 10 red Lawrence lines and 20 units of insulin zinc suspension daily.

On examination her weight was 15 st. 10½ lb. (100 kg.). The cranial nerves were intact. The fundi showed many hard exudates and haemorrhages, and arteriovenous nipping. The heart was enlarged to the left, the sounds were normal, and the blood-pressure was 180/110. The jugular venous pressure was not raised. There was pitting oedema of the legs extending to the mid-thigh. Initial serum electrolytes were normal and the blood urea was 74 mg./100 ml. The urine contained albumin and a few pus cells, but was sterile. The E.S.R. was 30 mm. in the first hour (Westergren). Serum protein estimations showed a total protein of 4.7 g./100 ml. (albumin 2.6 g., globulin 2.0 g.) (Biuret method), and there was an increase in the alpha$_2$-globulin fraction. Zinc sulphate turbidity was 2 units. There was 5 g. of protein per litre of urine (Esbach method).

She was well stabilized and aketotic on 10 black and 10 red lines and 20 units of insulin zinc suspension daily; however, she continued to have albuminuria averaging 9 g./l. each day. On January 16, 1962, the serum albumin had fallen to 1.2 g., the serum globulin was 2.8 g./100 ml., and the blood urea was 76 mg./100 ml.

In an attempt both to raise the serum albumin (Fister and Benas, 1960; Singh *et al.*, 1961) and to avoid the anticipated difficulties of insulin administration on discharge, it was decided that tolbutamide should be substituted for insulin. The insulin zinc suspension was stopped on January 17 after a dose of 20 units at 7 a.m. At 8 a.m. the following day she was given 1 g. of tolbutamide, and this was repeated at 2 p.m. At 4.45 p.m., after tea at 3.45 p.m., she was noted to be comatose and sweating profusely. She was promptly given 60 ml. of 40% glucose intravenously and recovered rapidly. Tolbutamide was withheld that evening and the urine was sugar-free during the night and next morning. She was rational and ate her meals normally. At 8 a.m. on January 19, 1 g. of tolbutamide was given, and at 5 p.m. the same day she again became hypoglycaemic, the blood sugar being 40 mg./100 ml. Further intravenous glucose was given and she recovered. She was restabilized on 20 units of insulin zinc suspension daily, but on January 21 had a myocardial infarct and died. Permission for necropsy was refused.

DISCUSSION

Mild hypoglycaemic symptoms are quite common in patients established on tolbutamide. In one large series symptoms attributable to hypoglycaemia were found in 6% of cases treated (Stowers and Bewsher, 1962). "One or two deaths have occurred in old people apparently from hypoglycaemia" (*B.M.J.*, 1957), but there are few reports of hypoglycaemic coma occurring (Schwartz, 1961). However, McKendry (1957) described a fatal case of hypoglycaemia in an elderly arteriosclerotic malnourished woman who had previously been hypoglycaemic on insulin; he cautioned against the use of tolbutamide in these circumstances. Severe and prolonged hypoglycaemic coma has been reported in the treatment of Parkinsonism with tolbutamide (Yonet and Ballard, 1961). Cosnett (1961) described irreversible cerebral damage following tolbutamide "overdosage."

One can speculate that in certain patients there is a sensitivity to tolbutamide and an overreaction of the remaining islet cells and subsequent severe and dangerous hypoglycaemia. We feel that under these circumstances the introduction of tolbutamide, particularly after insulin therapy, should be done only under hospital conditions. The correction of any untoward hypoglycaemia can be prompt and life-saving under such conditions. Little recognition of this complication of tolbutamide therapy has been given in the British literature, and the makers of tolbutamide have not mentioned this as a complication in their recent publications.

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